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Assessing the Impact of Renal Impairment on Outcome after Arterial Intervention: A Prospective Review of 1559 Patients

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Aim. *To investigate the impact of pre and peri-operative renal impairment on outcome, and the need for renal replacement therapy, in a multicenter study of patients undergoing a variety of surgical and radiological arterial procedures.*
Methods. *A six month prospective multi-centre study of 1559 consecutive patients undergoing arterial interventions was performed. The primary outcome measures were the development of renal impairment, 30 day mortality and the need for renal replacement therapy. CRI was defined as an admission serum Creatinine > 125 μmol/l. ARI was defined as a rise in serum Creatinine of >50% above pre-operative levels, excluding patients in whom the post operative level remained <125 μmol/l. A multivariate logistic regression model was constructed to identify independent risk factors for the development of ARI and mortality.*
Results. *There was a significantly increased 30 day mortality in those patients who developed ARI (29/90 − 32%) or who had CRI (43/269 − 16%) when compared with those whose creatinine remained normal throughout (44/1200 − 4%) ($p < 0.0001$ − Chi-square test). One thousand two hundred and ninety patients had normal pre operative renal function and 269 patients had CRI. Seven percent (90/1290) of the patients with normal pre-operative creatinine developed ARI. Operation type, emergency presentation, and chronic renal impairment were independent predictors of both acute renal impairment ($p < 0.01$) and mortality ($p < 0.001$). Sixteen patients (1%) required temporary haemofiltration (in 9 patients this developed in the context of multiple organ failure) with only 1 requiring long term support. Eleven of these patients died (30 day mortality 69%).*
Conclusions. *Renal failure following arterial intervention is associated with significant mortality. Renal replacement therapy is necessary mainly in the setting of multiple organ failure on intensive care units with few patients surviving to require long term renal replacement therapy. The identification of the 'at risk' patient is most strongly associated with age, raised preoperative creatinine, emergency procedures and thoraco-abdominal aneurysm.*

Keywords: Renal failure; Aortic surgery; Risk factor; Haemodialysis.

Introduction

A relationship between renal failure and increased mortality following surgery is well recognized.[1,2] In vascular surgery several studies have shown that an independent relationship exists between renal impairment pre-operatively and an increased risk of post operative death in patients undergoing open repair of abdominal and thoracic aneurysms.[1–3] These procedures involve the additional renal insult of an aortic cross clamp. Vascular patients, by the systemic nature of the underlying disease process and the high proportion of diabetics, are recognized to have an increased prevalence of concomitant renal disease.[4] These patients are routinely optimized from both a cardiac and respiratory point of view, but renal optimization is far more complex and difficult to achieve. As a result it has been suggested that every vascular unit should have specialist renal unit support and easy access to dialysis facilities. This study was performed to assess the impact of pre and peri-operative renal impairment on patient outcome, specifically mortality. The study was also designed to assess the requirements for post operative renal support and identify risk factors, if any, associated with the development of post operative acute renal impairment.

Patients and Methods

Prospective data, over a six month period, was collected on 1559 (1057 male and 502 female) consecutive patients with a median age of 71 years (range of

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16 to 98) from 11 United Kingdom vascular units who underwent either open or interventional radiological procedures, including endovascular exclusion of infra-renal aneurysm (EVAR). Data collection used a standard proforma for patient demographics, diagnoses, operations performed, timing of intervention as well as risk factors for both vascular and renal disease and outcome. Table 1. The proforma data was collated by unit research nurses and returned to a single researcher who checked forms for incomplete or missing data.

Renal function was assessed using serum creatinine as it was not routine practice in these units to measure GFR pre-operatively. A normal serum creatinine was defined as an admission creatinine < 125 μmol/l as per the normal range quoted by biochemical laboratories. Pre operative chronic renal impairment (CRI) was defined as a value greater than 125 μmol/l. Post operative acute renal impairment (ARI) was defined as an increase in serum creatinine to 50% above the base line, and to a level greater than 125 μmol/l. This equates to an approximation in fall in GFR, for a 70 kg male, from 60 to 40 ml/min.

The primary study endpoints were pre and maximum post operative serum creatinine, 30 day mortality and any requirement for post-operative renal replacement therapy using either haemofiltration or haemodialysis.

Statistical Analysis

Binary logistical regression models were created for dependent co-factors of acute renal impairment and 30 day mortality. Co- variates in both models are shown in Table 1. In the analysis of mortality model renal impairment was also included. Analysis was performed using SPSS version 10 for Microsoft Windows.

Results

Operative procedures

The procedures performed in this cohort of 1559 patients are shown in Table 2. The highest mortality follows the emergency procedures − (IRAAA repair, embolectomy amputation) and thoraco-abdominal aneurysm repair. The highest incidence of peri-operative renal impairment follows supra-renal aortic cross-clamp placement for thoracoabdominal aneurysm repair with 47% incidence of ARI. The radiological patients underwent angioplasty with or without stenting. The endovascular group consisted of patients in whom stent grafts were deployed in an infra-renal aneurysm. Operative procedures with small numbers ('other') have not been analysed separately and include extra-anatomical bypasses, open thrombectomies and endarterectomies of vessels other than the carotids. The high mortality of this group represents the fact that many were emergency procedures.

Table 1. Pre-operative risk factors recorded and included in binary logistical regression model

Pre operative factors	Drug history
Diabetes mellitus	NSAID
Hypercholesterolaemia	ACE inhibitor
Hypertension	Metformin
Angiography in preceding one week	

Renal impairment

One thousand two hundred and ninety (83%) patients had normal pre operative renal function and of these, 7% (90/1290) developed ARI. 269 (17%) patients had CRI. The 30 day mortality of all patients was 8% (117/1559). In patients who had normal creatinine pre-operatively and where this remained normal mortality was 4% (44/1200). In those patients who had pre-operative CRI, mortality was significantly higher at 17% ($p < 0.0001$). The highest mortality was seen in patients who developed peri-operative ARI on a background of normal pre-operative renal function where mortality was 32% ($p < 0.0001$). The groups and their outcomes are shown in Fig. 1. There was no significant difference in risk factors between these groups, shown in Table 3.

Renal replacement therapy

Sixteen patients (1%) required temporary haemofiltration: in the majority (9 patients) this developed in the context of multiple organ failure. Eleven of these patients died (30 day mortality 69%). In 4 patients renal function recovered and only 1 patient went on to require long term renal support. In this group 6 had normal preoperative creatinine with 3 having emergency procedures (IRAAA; bilateral femoral embolectomies; Aorto-bifemoral bypass) and 3 elective procedures (TAAA (2) and elective IRAAA). Of those with preoperative CRI, 6 had emergency procedures (IRAAA; Embolectomy; removal infected aortic graft; fem-pop bypass; fem-anterior tibial bypass) and 4 elective procedures (TAAA (2); IRAAA (2)).

Multivariate logistical regression analysis

Binary logistical regression showed significance for mode of presentation (urgent/emergency), age,

Table 2. Incidence of chronic renal impairment (CRI), acute renal impairment (ARI) and mortality by procedural sub group

Procedure	N	Mortality (All)	CRI	Mortality (CRI)	ARI	Mortality (ARI)
Thoraco-abdominal aneurysm repair*	23	17%(4/23)	17%(4/23)	50%(2/4)	47%(9/19)	11%(1/9)
Emergency Aneurysm Repair*	101	35%(35/101)	32%(32/101)	47%(15/32)	17%(12/69)	42%(5/12)
Elective Aneurysm Repair*	185	7%(13/185)	24%(45/185)	9%(4/45)	16%(23/141)	17%(4/23)
Endovascular stent graft (EVAR)	47	0%(0/47)	13%(6/47)	0%(0/6)	2%(1/41)	0%(0/1)
Infra-inguinal bypass	355	5%(18/355)	17%(59/355)	12%(7/59)	4%(12/296)	50%(6/12)
Aorto-iliac bypass	129	7%(9/129)	9%(11/129)	27%(3/11)	5%(5/103)	60%(3/5)
Lower limb embolectomy*	85	15%(13/85)	22%(19/85)	37%(7/19)	14%(9/66)	56%(5/9)
Radiological intervention	137	1%(1/137)	9%(12/137)	0%(0/12)	3%(3/101)	33%(1/3)
Carotid Intervention	223	1%(1/223)	13%(30/223)	3%(1/30)	1%(2/209)	0%(0/2)
Amputations	148	9%(13/148)	16%(23/148)	9%(2/23)	7%(9/137)	22%(2/9)
Other	126	9%(10/108)	22%(28/126)	11%(3/28)	4%(5/108)	40%(2/5)
Total	1559	8%(117/1559)	17%(269/1559)	17%(44/269)	7%(90/1290)	32%(29/90)

*Statistically significant predictors of ARI.

operation type and chronic renal impairment as predictors of acute renal impairment ($p < 0.001$ for all). Acute renal impairment and chronic renal impairment where independently associated with mortality as shown earlier. None of the risk factors of vascular and renal disease used in this study where associated with an increased risk of acute renal impairment.

Discussion

The impact of renal failure on surgical outcome has been well established for aortic surgery but not for aorto-iliac disease, lower limb bypass surgery and interventional radiology. Many patients will have impaired pre-operative renal function and are exposed to contrast, hypotension, sepsis, hypoxia and cholesterol embolisation and reperfusion of ischaemic tissue. Post operative acute renal failure is associated with increased mortality.

In high risk patients, for example thoracoabdominal aortic aneurysm repair the incidence of ARI is as high as 40%.[5] Nevertheless in this high risk group the requirement for renal support with haemofiltration was significantly less likely. In Stanley Crawford's study of 1525 patients 5.5% (1 in 20) required renal support.[6]

In another published study of 440 patients undergoing elective or emergency infra-renal abdominal aortic aneurysm repair acute renal failure occurred in 32 patients (7.3%). Twenty of these patients (62.5%) died.[7]

Recently published data on 130 patients who underwent Crawford type IV thoraco-abdominal aneurysm repair and 44 patients who had juxta-renal

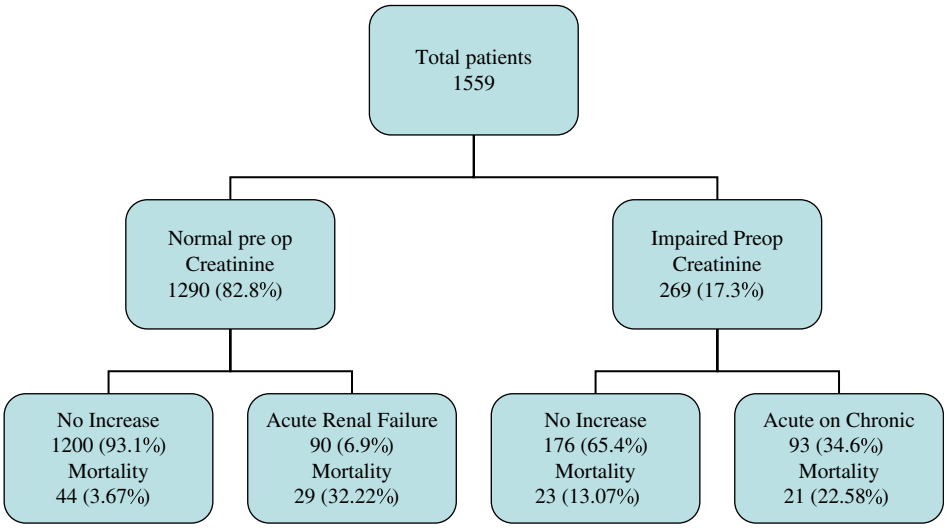

Fig. 1. Renal function and mortality in 1559 patients.

Table 3. Demographic data of the separate outcome groups

	Normal Pre & Post	Acute renal impairment (ARI)	Chronic renal impairment (CRI)	*p*-value
N	1200	90	269	
Gender	M: 788 F: 412	M: 56 F: 34	M: 213 F: 56	
Age (median)	70	73	74	
Diabetes Mellitus	17%	20%	18%	Ns
Hypertension	39%	46%	50%	Ns
Cholesterol	10%	11%	9%	Ns
NSAID	16%	13%	14%	Ns
ACE Inhibitor	6%	6%	10%	Ns
Metformin	2%	8%	5%	Ns
Angiogram	13%	17%	12%	Ns

aneurysm repair has shown that raised pre-operative serum creatinine concentration predicted mortality. Previous work has established age >50 years, pre-operative serum creatinine > 120 μmol/L, >5 unit blood transfusion, visceral perfusion, left renal artery reattachment, simple cross-clamp technique and left heart bypass as all predictive of ARI.[8]

There is no standard definition for renal impairment and a definition used in a previously published study on renal failure in vascular surgery was used.[3,9] The correlation between peri-operative serum creatinine and creatinine clearance has been established with increases of greater than 20% in baseline creatinine identifying most patients whose clearance fell by more than 50%. Previous studies have demonstrated a correlation between serum creatinine and GFR in surgical patients.[10] It was not feasible to measure creatinine clearance in so large a patient group and data, allowing the use of the Cockgroft-Gault formula for GFR, was not collected.

The association of peripheral vascular disease with renal impairment is well recognized;[11] the association has been shown to be independent of potential confounders such as age, diabetes, hypertension, coronary artery disease, stroke history, and hypercholesterolemia. Little has been published on the impact of renal impairment on short-term outcomes after lower limb bypass. In this study the incidence of acute renal failure following aorto-iliac and infra-inguinal procedures were both less than five percent. The Department of Veterans Affairs' National Surgical Quality Improvement Program (NSQIP) showed that moderate renal insufficiency (estimated GFR 30–60 ml/min) was associated with an increased incidence of mortality.[1]

The incidence of acute renal failure in lower limb bypass was 3 percent in this study. Few good studies have been published. In one series of 302 consecutive lower limb angiograms (84% diagnostic) 46% of the patients had pre-existing renal impairment (creatinine > 118 μmol/l), of whom 11% were on dialysis. Contrast nephropathy occurred in 5 percent of procedures and was associated with a mortality of 6%. Precautions to avoid contrast nephropathy were taken in only 2 cases.[12] In 213 consecutive patients undergoing infra inguinal angioplasty acute renal dysfunction was reported in 12% of patients. Pre-existing impaired renal function and contrast dosages were independent predictors of acute renal failure in that study.[13] In the current series the mortality from interventional procedures was less than one percent which may reflect better awareness of the risk of contrast nephropathy. No data was collected in this study on contrast usage and we were unable to obtain this retrospectively. A recently published randomized trail has suggested that N-acetylcysteine confers no additional protective benefit prior to contrast administration.[14]

The sub group of patients undergoing endovascular procedures in this study is too small for analysis. Data on 164 patients undergoing endovascular stent grafting has shown that of the 9% of patients with preoperative renal failure, 47% died. In patients with preoperative renal impairment, the perioperative mortality rate was 27%.[15]

This study failed to identify predictive risk factors for acute renal impairment other than pre-existing chronic renal impairment, mode of presentation and procedure type. A systematic review of 28 studies that examined preoperative risk factors for postoperative renal failure in 11,000 surgical patients came to the same conclusion. These studies included vascular operations and considered thirty variables.[9] Unsurprisingly several operative sub groups have a high incidence of acute renal failure.

There has been an increasing awareness over the last few years that renal impairment results in increased morbidity and mortality in patients independent of other risk factors. However the majority of studies have focused on patients with known renal impairment or those already receiving dialysis. There was therefore little information on the far larger group of patients with previously normal renal function. High risk patients are difficult to predict pre-operation. Preoperative angiography and drug treatment with potentially nephrotoxic drugs such as metformin were not associated with an increased risk of renal impairment.

Arterial surgery insults the kidney in several ways. The most obvious single factor is renal ischaemia secondary to supra renal aortic cross clamping. Further factors which are implicated in renal impairment are intraoperative hypotension, blood transfusion and atheroembolism.

The requirement for renal replacement therapy was low in this series of patients, with only sixteen patients requiring temporary dialysis and only one patient going onto require long term renal support. This is in part related to the extremely high mortality of patients who developed renal impairment.

This study supports previous work that suggested renal impairment has a significant impact on post operative mortality; and particularly in those with impaired preoperative renal function. This needs to be carefully considered when weighing up the benefit of surgery in these patients for operative intervention. Nevertheless it is difficult to justify the assertion that most vascular units require the support of a specialist renal unit in the same centre, as the requirement for chronic renal support is extremely low. However provision should be made for transfer of those patients who are likely to require renal support.

Conclusion

Renal failure, both pre and peri-operatively is associated with significant mortality. Renal replacement therapy is necessary mainly in the setting of multiple organ failure on intensive care units with few patients surviving to require long term renal replacement therapy. The identification of the 'at risk' patient is not easy, other than considering as high risk certain procedures and all patients with raised pre-operative creatinine. Patients with evidence of renal impairment need early identification and appropriate multidisciplinary support.

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